Cardiac fibroblasts regulate myocardial proliferation through beta1 integrin signaling.

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Authors: Masaki Ieda, Takatoshi Tsuchihashi, Kathryn N Ivey, Robert S Ross, Ting-Ting Hong, Robin M Shaw, Deepak Srivastava

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Public Summary:

Scientific Abstract:
Growth and expansion of ventricular chambers is essential during heart development and is achieved by proliferation of cardiac progenitors. Adult cardiomyocytes, by contrast, achieve growth through hypertrophy rather than hyperplasia. Although epicardial-derived signals may contribute to the proliferative process in myocytes, the factors and cell types responsible for development of the ventricular myocardial thickness are unclear. Using a coculture system, we found that embryonic cardiac fibroblasts induced proliferation of cardiomyocytes, in contrast to adult cardiac fibroblasts that promoted myocyte hypertrophy. We identified fibronectin, collagen, and heparin-binding EGF-like growth factor as embryonic cardiac fibroblast-specific signals that collaboratively promoted cardiomyocyte proliferation in a paracrine fashion. Myocardial beta1-integrin was required for this proliferative response, and ventricular cardiomyocyte-specific deletion of beta1-integrin in mice resulted in reduced myocardial proliferation and impaired ventricular compaction. These findings reveal a previously unrecognized paracrine function of embryonic cardiac fibroblasts in regulating cardiomyocyte proliferation.